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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/734,049	12/12/2003	Kyogo Itoh	Q-78382	2555

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EXAMINER	
GODDARD, LAURA B	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 03/16/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/734,049	ITOH ET AL.	
	Examiner	Art Unit	
	Laura B. Goddard, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 January 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *37-56* is/are pending in the application.

4a) Of the above claim(s) *44-48, 51-55* is/are withdrawn from consideration.

5)☒ Claim(s) *37,39 and 56* is/are allowed.

6)☒ Claim(s) *38,40-43,49 and 50* is/are rejected.

7)☒ Claim(s) *37,50 and 56* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2/10/06, 2/26/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *PTO-90C, Sequence non-comply*.

DETAILED ACTION

1. The Election filed January 25, 2006 in response to the Office Action of December 28, 2005 is acknowledged. Applicant elected partially with traverse Group I, drawn to an isolated polypeptide consisting of SEQ ID NO:188 and pharmaceutical composition and cancer vaccine comprising said polypeptide (new claims 37-42).

Applicants request that a reasonable number of polypeptide sequences be examined in this application and provisionally elect 5 amino acid sequences. Applicants argue that the polypeptide and peptide sequences are related and would not constitute undue burden. Applicants cite a passage from MPEP 803.04 to support their argument for searching a reasonable number of sequences, see pages 10-11 of the Election filed January 25, 2006.

The argument has been considered but has not been found persuasive because each polypeptide or peptide of the instant application consists of a structurally and functionally different sequence and is considered an independent and distinct invention. To clarify the passage cited from MPEP 803.04, Examiner has copied the passage in entirety:

"Polynucleotide molecules defined by their nucleic acid sequence (hereinafter "nucleotide sequences") that encode different proteins are structurally distinct chemical compounds. **These sequences are thus deemed to normally constitute independent and distinct inventions within the meaning of 35 U.S.C. 121. Absent evidence to the contrary, each such nucleotide sequence is presumed to represent an independent and distinct invention, subject to a restriction**

requirement pursuant to 35 U.S.C. 121 and 37 CFR 1.141 et seq. Nevertheless, to further aid the biotechnology industry in protecting its intellectual property without creating an undue burden on the Office, the Director has decided *sua sponte* to partially waive the requirements of 37 CFR 1.141 et seq. and permit a reasonable number of such nucleotide sequences to be claimed in a single application. See Examination of Patent Applications Containing Nucleotide Sequences, 1192 O.G. 68 **(November 19, 1996).**

It has been determined that normally ten sequences constitute a reasonable number for examination purposes. Accordingly, in most cases, up to ten independent and distinct nucleotide sequences will be examined in a single application without restriction. In addition to the specifically selected sequences, those sequences which are patentably indistinct from the selected sequences will also be examined. Furthermore, nucleotide sequences encoding the same protein are not considered to be independent and distinct inventions and will continue to be examined together. In some exceptional cases, the complex nature of the claimed material, **for example a protein amino acid sequence reciting three dimensional folds, may necessitate that the reasonable number of sequences to be selected be less than ten**. In other cases, applicants may petition pursuant to 37 CFR 1.181 for examination of additional nucleotide sequences by providing evidence that the different nucleotide sequences do not cover independent and distinct inventions."

Examiner points out that the Director partially waived requirements of 37 CFR 1.141 et seq. to "permit a reasonable number of such nucleotide sequences to be

claimed in a single application" **in 1996.** The size of the sequence and literature database required to search a single sequence has exponentially increased every year for **10 years** since the Director's statement. A search for more than one amino acid sequence would not necessarily result in or overlap the search of another sequence and the current size of the sequence database clearly creates undue burden on the Office. For these reasons, the restriction requirement is deemed to be proper and is therefore made FINAL.

Rejoinder

2. Applicant has requested rejoinder for new claims 43-55. Claim 37, as drawn to an isolated peptide consisting of SEQ ID NO:188, has been found allowable.

In the interest of compact prosecution, process claims that use the allowable product of claim 37 have been rejoined for examination purposes. Claims 43, 49, and 50 are process claims that depend from or otherwise includes all the limitations of the patentable product of Group I. In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims are withdrawn, and the rejoined process claims are fully examined for patentability in accordance with 37 CFR 1.104. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined and these claims include 52 and 53 drawn to a method of using the cancer vaccine, and 54 and 55 drawn to a method of using the pharmaceutical composition. Claims drawn to the pharmaceutical composition and cancer vaccine have

not been found allowable, hence claims 52-55 have not been rejoined for examination. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). The requirement for restriction between claims 43, 49, and 50 and Group I as drawn to an isolated peptide consisting of SEQ ID NO:188, is withdrawn and claims 43, 49, and 50 are hereby rejoined with Group I.

3. Claims 1-36 were canceled. Claims 37-56 were added. New claim 56 drawn to a reagent kit comprising a peptide of claim 37 will be joined with Group I for examination. Since applicant has elected Group I, drawn to an isolated polypeptide consisting of SEQ ID NO:188 and pharmaceutical composition and cancer vaccine comprising said polypeptide (new claims 37-42), for action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, the embodiments of claims 44-47 directed to a polynucleotide, claim 48 directed to an antibody, and claims 51-55 directed to methods have been withdrawn from consideration as being directed to a non-elected invention. See 37 C.F.R. § 1.142(b) and M.P.E.P. § 821.03. Newly submitted claims 44-48 and 51-55 are directed to an invention that is independent or distinct from the invention originally claimed for the reasons previously set forth in the restriction requirement mailed December 28, 2005, see pages 7-12.

Claims 37-43, 49, 50, and 56 are currently under prosecution.

Specification

4. The disclosure is objected to because it does not comply with the sequence rules:

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.8821 (a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reasons(s) set forth on the attached Notice to Comply with Requirements for Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. **In particular, no sequence identifier is associated with the sequences disclosed in the Drawings including Figures 11, 13 a, b, and on page 70 of the specification.** Applicant must correct these informalities.

Applicant is given the period of reply for this Action within which to comply with the sequence rules, 37 CFR 1.821-1.825. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 CFR 1.821 (g). Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 CFR 1.136(a). In no case may an applicant extend the period for response beyond the SIX MONTH statutory period. Direct the response to the undersigned. Applicant is requested to return a copy of the attached Notice to Comply with the response.

5. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code, see pages 18, 29, 56, and 57. Applicant is

required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Claim Objections

6. Claims 37, 50 and 56 are objected to for containing subject material that is drawn to a non-elected invention. Claims 37 and 50 recite SEQ ID NOs other than the elected SEQ ID NO:188 and claim 56 recites "an antibody that immunologically recognizes...harboring said expression vector". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 49 and 50 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: a control measurement of IFN-γ production in the absence of the test compound, comparing the control measurement with the IFN-γ measurement in the presence of the test compound, and a correlation step describing how the results of the assay relate back to the preamble of the method objectives, for example, wherein an increase in the IFN-γ production in the presence of the test compound identifies a compound that enhances recognition of the peptide.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claim 38 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for **an isolated peptide fragment of claim 37 wherein said peptide fragment is recognized by a cytotoxic T lymphocyte in an HLA-A2 restricted manner and/or induces a cytotoxic T lymphocyte in an HLA-A2 restricted manner** does not reasonably provide enablement for an isolated peptide fragment of claim 37 wherein said peptide fragment is recognized by a cytotoxic T lymphocyte and/or induces a cytotoxic T lymphocyte. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The claims are drawn to an isolated peptide fragment of claim 37 wherein said peptide fragment is recognized by a cytotoxic T lymphocyte and/or induces a cytotoxic T lymphocyte, this means the claims are drawn to an isolated peptide fragment of claim 37 wherein said peptide fragment is recognized by a cytotoxic T lymphocyte and/or induces a cytotoxic T lymphocyte regardless of how the peptide is presented to the a cytotoxic T lymphocyte (with or without an HLA molecule).

The specification discloses that cytotoxic T lymphocytes (CTLs) recognize a complex consisting of an HLA molecule and a tumor antigen peptide, wherein the CTLs recognize the tumor cells in an HLA-restricted manner. HLA is classified into class I and

II antigen and within HLA class I antigens, there are further classifications into HLA-A, HLA-B, HLA-C, and so on. Within HLA-A, there are genetic polymorphisms that result in a diversity of HLA-A antigens such as A1, A2, A24, A26, and so on (p. 2). The specification discloses that the claimed peptide, SEQ ID NO:188, was identified as an HLA-A2 restricted tumor antigen peptide through a motif search for peptides capable of binding to the HLA-A2 molecule, were recognized by OK-CTLd in an HLA-A2-restricted manner and enhanced IFN-γ production from OK-CTLd (p. 57 and 58, Example 3). OK-CTL is an HLA-A2-restricted tumor-specific CTL established from a colon cancer patient (p. 52-53, Example, 1).

One cannot extrapolate the disclosure of the specification to the scope of enablement of the claims because the specification discloses that CTLs recognize a complex consisting of an HLA molecule and a tumor antigen peptide, wherein the CTLs recognize the tumor cells in an HLA-restricted manner. Considering the disclosure, a CTL could not recognize the peptide SEQ ID NO:188 unless it was complexed to an HLA molecule, and the HLA molecule that binds SEQ ID NO:188 is HLA-A2.

Reasonable correlation must exist between the scope of the claims and scope of enablement set forth, and it cannot be reasonably predicted that an isolated peptide SEQ ID NO:188 could be recognized by a CTL and/or induce a CTL as broadly claimed. Therefore, in view of the lack of guidance from the specification, the breadth of the claims and the absence of working examples, it would require undue experimentation for one skilled in the art to practice the invention as broadly claimed.

9. Claims 40-43 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are drawn to a pharmaceutical composition comprising the peptide fragment of claim 37 (claim 40), a cancer vaccine comprising an immunoprotective amount of the peptide of claim 37 and a pharmaceutically acceptable carrier (claim 41), wherein said cancer vaccine is effective for one or more cancers listed in claim 42, and a method for inducing a cytotoxic T lymphocyte comprising contacting the peripheral blood mononuclear cells with the peptide of claim 37 (claim 43).

The specification discloses that SEQ ID NO:188 was produced from a cDNA library of a human colon cancer cell line which was identified as an antigen that is recognized by OK-CTLd (p. 16). The specification discloses that the claimed peptide, SEQ ID NO:188, was identified as an HLA-A2 restricted tumor antigen peptide through a motif search for peptides capable of binding to the HLA-A2 molecule, was recognized by OK-CTLd in an HLA-A2-restricted manner, and enhanced IFN-γ production from OK-CTLd (p. 57 and 58, Example 3), wherein OK-CTL is an HLA-A2-restricted tumor-specific CTL established from a colon cancer patient (p. 52-53, Example, 1). The peptide SEQ ID NO:188 was pulsed to T2 cells expressing HLA-A2 followed by culturing the T2 cells with OK-CTLd to measure IFN-γ production from OK-CTLd.

Peptides recognized by OK-CTLd were selected using the amount of IFN-γ production as an index (p. 29).

The specification discloses that not everyone expresses HLA-A2 antigens because it is an allele found in only a certain percentage of different ethnic groups (p. 47), and that a pharmaceutical composition comprising the claimed peptide would be effective for treating cancer in patients expressing HLA-A2 (p. 47). The specification further discloses that peripheral blood mononuclear cells (PBMC) derived from an HLA-A2 expressing colon cancer patient recognized some HLA-A2 restricted tumor antigens but PBMCs from a metastatic melanoma patient or healthy donor did not recognize the antigens (p. 31). The polypeptides or peptides that were recognized by the PBMCs from the colon cancer patient and induced IFN-γ production are listed on pages 65 and 66. SEQ ID NO:188 is not listed as a peptide that was recognized by PBMCs. The specification discloses that tumor antigens shown in Tables 1 to 7, which **does not** include SEQ ID NO:188, would be suitable for use in the specific immunotherapy of HLA-A2 positive colon cancer patients.

Finally, the specification discloses that a cancer vaccine means a medicament capable of damaging a cancer cell selectively by inducing and/or enhancing a specific immunological response to a cancer cell (p. 48).

One cannot extrapolate the teaching of the specification to the enablement of the claims because the specification does not provide any guidance or examples for a pharmaceutical composition or vaccine comprising peptide SEQ ID NO:188 enabled for treating any cancer or treating any patient regardless of whether they express the HLA-

A2 allele. It is clear that peptide SEQ ID NO:188 is an HLA-A2 restricted antigen and that it is recognized by a CTL in a HLA-A2 restricted manner *in vitro*, however, the specification does not provide guidance or support for the claimed peptide to predictably function in treating cancer in a pharmaceutical composition or cancer vaccine. Additionally, one could not predictably induce a cytotoxic T lymphocyte comprising contacting PBMCs with the claimed peptide SEQ ID NO:188 because the specification does not disclose that this peptide was recognized by PBMCs derived from either colon cancer, melanoma cancer, or healthy subjects.

The specification discloses that a tumor antigen can be used for cancer vaccine therapy through the action of inducing and/or activating CTL (p. 3 and 79), however Chaux et al, (Int J Cancer, 1998, 77: 538-542) teach some of the CTLs have an affinity that is too low for the recognition of cells that have processed the antigen, which is different from the *in vitro* condition in which the synthetic peptides are in high number when incubated with the cells (p.541, second column, second paragraph). Given the above, even if a peptide on a cell line cell was recognized by T-cells *in vitro*, it could not be predicted that the T-cells would recognize these peptides *in vivo* and if not recognized *in vivo*, it is clear that one would not know how to use the claimed peptide in a pharmaceutical composition or cancer vaccine. Kirkin et al (1998, APMIS, 106 : 665-679) teach that in particular for tumor antigens, for some antigens, due to the existence of self-tolerance, only T cells with low affinity T-cell receptors are produced (abstract). Similarly Sherman et al, (Critical Reviews in Immunol, 1998, 18:47-54) teach that self-tolerance may eliminate T cells that are capable of recognizing T-cell epitopes with high

avidity . Smith (Clin Immunol, 1994, 41(4): 841-849), teaches that antigen overload, due to antigen shedding by actively growing tumor, could block specifically either cytotoxic or proliferative responses of tumor specific T cells (p. 847, last paragraph bridging p.848 and p.848). Smith further teaches that many tumors progressively lose MHC representation at the surface of the cell, and the loss could severely limit the possibilities for cytotoxic T cells specific for a tumor specific antigen to find said tumor specific antigen in the necessary MHC context (p.484). In particular as drawn to the peptide itself, Bossart et al (Blood, 1999, 93:4309-4317) are very clear that immunization methods using self-antigens have often resulted in the induction of low-affinity CTL responses and consequently a lack of sufficient recognition of naturally processed antigens by these CTL. Presentation of antigens by APC may be critical for the effectiveness of an induced immune response (p. 4309, col 1). However, given the teachings set forth above and the known state of the art at the time the invention was made, one would not believe it more likely than not that the claimed pharmaceutical composition and cancer vaccine would function as claimed.

In addition, as drawn to cancer vaccines, Boon (Adv Can Res, 1992, 58:177-210) teaches that for active immunization in human patients we have to stimulate immune defenses of organisms that have often carried a large tumor burden. In addition, Boon teaches that even if activated CTLs are significantly increased, the therapeutic success remains unpredictable due to inconsistencies in antigen expression or presentation by tumor cells (p.178, paragraph before last paragraph). Thus based on the teaching in the art and in the specification, one cannot predict that an adequate *in vivo* T cell response

useful for immunotherapy, as contemplated, could be induced by the peptide of the invention in patients having tumor burden. In addition, as drawn to peptide tumor vaccines for the induction of a T-cell response, Kirkin et al, *Supra* review several melanoma-associated antigens, including NY-ESO1, conclude that initiation of a strong immune response *in vivo* is an extremely rare event (p.674, first column, last paragraph). Kirkin et al teach that for some antigens, due to the existence of self-tolerance, only T cells with low affinity T-cell receptors are produced (abstract). Kirkin et al teach that although several peptides of melanoma associated antigens have been identified as recognized by CTL *in vitro*, and peptides from MAGE-A1 and MAGE-A3 have been tested for their ability to induce anti-melanoma immune response *in vivo*, only one of the peptides, peptide EVDPIGHLY of MAGE-A3, has limited anti-tumor activity, indicating their low immunogenicity (p.666, second column, second paragraph, last 6 lines). Further, even this peptide EVDPIGHLY of MAGE-A3 produces a very low level of CTL response which is detectable only by a very sensitive method, as taught by Chaux et al, *Supra*.

The specification provides no working examples which would provide guidance to one skilled in the art and no evidence has been provided which would allow one of skill in the art to predict that the claimed invention would function as claimed or as contemplated with a reasonable expectation of success. Given the lack of guidance for a method of inducing a CTL comprising contacting PBMCs with SEQ ID NO:188 and given the unpredictability that the pharmaceutical composition or cancer vaccine comprising SEQ ID NO:188 would elicit an adequate T cell response *in vivo*, useful for

the treatment of cancer as contemplated, the lack of adequate disclosure in the specification, and in view of the complex nature of the claimed invention, one of skill in the art would be forced into undue experimentation to practice the claimed invention.

Conclusion

10. Claims 37, 39, and 56 as drawn to an isolated peptide consisting of SEQ ID NO:188, wherein said peptide is recognized by a cytotoxic T lymphocyte in an HLA-A2 restricted manner, and/or induces a cytotoxic T lymphocyte in an HLA-A2-restricted manner, and a reagent kit comprising SEQ ID NO:188 and a buffered solution are allowed. Claims 38, 40-43, 49, 50 are rejected.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Laura B. Goddard, Ph.D. whose telephone number is (571) 272-8788. The examiner can normally be reached on 8:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Laura B Goddard, Ph.D.
Examiner
Art Unit 1642

GARY B. NICKOL, PH.D.
PRIMARY EXAMINER

UNITED STATES DEPARTMENT OF COMMERCE
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APPLICATION NO./ CONTROL NO.	FILING DATE	FIRST NAMED INVENTOR / PATENT IN REEXAMINATION	ATTORNEY DOCKET NO.
10/734049	12/12/03	Kyogo Itoh	Q-78382

EXAMINER	
Laura B. Goddard	
ART UNIT	**PAPER**
1642	2

DATE MAILED:

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner for Patents

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.8821 (a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reasons(s) set forth on the attached Notice to Comply with Requirements for Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.
Applicant is given ONE MONTH, or THIRTY DAYS, whichever is longer from the date of this letter within which to comply with the sequence rules, 37 CFR 1.821-1.825. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 CFR 1.821 (g). Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 CFR 1.136(a). In no case may an applicant extend the period for response beyond the SIX MONTH statutory period. Direct the response to the undersigned. Applicant is requested to return a copy of the attached Notice to Comply with the response.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Laura B. Goddard, Ph.D. whose telephone number is (571) 272-8788. The examiner can normally be reached on 8:00am-5:00pm.
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.
Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Laura B Goddard, Ph.D.ExaminerArt Unit 1642

Application No. 10/734049

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 CFR 1.821 - 1.825 for the following reason(s):

☒ 1. This application clearly fails to comply with the requirements of 37 CFR 1.821 - 1.825. Applicant's attention is directed to these regulations, published at 1114 OG 29, May 15, 1990 and at 55 FR 18230, May 1, 1990.

☒ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 CFR 1.821(c).

☒ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 CFR 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 CFR 1.822 and/or 1.823, as indicated on the attached copy of the marked-up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A substitute computer readable form must be submitted as required by 37 CFR 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable form of the "Sequence Listing" as required by 37 CFR 1.821(e).

☐ 7. Other: No SEQ ID NOs associated with sequences on Drawings Fig 11, 13a + 13b.

Applicant must provide:

☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing"

☒ An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 CFR 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d)

For questions regarding compliance with these requirements, please contact:

For Rules Interpretation, call (703) 308-1123
For CRF submission help, call (703) 308-4212
For PatentIn software help, call (703) 557-0400

Please return a copy of this notice with your response.